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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/700,434	02/28/2001	Wilfried Fischer	2727-130	5919

20999 7590 04/08/2005

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EXAMINER	
GOLLAMUDI, SHARMILA S	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 04/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/700,434	FISCHER, WILFRIED	
	Examiner	Art Unit	
	Sharmila S. Gollamudi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5,8,10-15,17-24 and 26-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,5,8,10-15,17-24 and 26-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination received December 9, 2004 is acknowledged. Claims **1, 4-5, 8, 10-15, 17-24, and 26-32** are pending in this application.

Response to Arguments

Applicant's arguments with respect to the claims have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4-5, 8, 10-15, 17-24, and 26-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites, "wherein the at least one active ingredient solution or dispersion is not miscible in water". The claims also recites that the system contains an optional active ingredient containing adhesive layer. It is unclear whether the at least one active ingredient in the polymer layer is water immiscible or the polymer layer and optional adhesive layer both contain a water immiscible active ingredient. If the applicant intends for only the polymer layer to contain the water immiscible active agent, then the examiner suggests placing this limitation (wherein the at least one active ingredient solution or dispersion is not miscible in water) after the recitation "dried layer" of component b.

Claim 5 depends from parent claim 1 and recites, "wherein the polymer layer is perforated, so that at least the adhesive layer above the polymer layer can come into contact with

the cover layer and the adhesive layer below the polymer layer." Independent claim 1 recites a transdermal system that comprises A) a cover layer B) a polymeric matrix, C) an optional adhesive layer, and D) a protective layer. Therefore, "the adhesive layer above the polymer layer" and "the adhesive layer" below the polymer layer lacks sufficient antecedent basis for this limitation in the claim since the parent claim only provides for one optional adhesive layer. Further, it is unclear if this claim in fact requires two separate adhesive layers (one below the polymer layer and one above the polymer layer).

Claim 10 recites a process of manufacturing the system wherein the adhesive layer is applied onto the protective layer, followed by applying the polymer layer, optionally applying the further adhesive layer above the polymer layer, and applying a cover layer. It is unclear whether the system has an adhesive layer or this is optional as in the parent claim or the system requires at least one adhesive layer and can optionally have two adhesive layers.

Further, clarification is required.

The examiner suggest rewording claim 32. The examiner suggests the following: The transdermal system according to claim wherein the system contains a mixture of at least two actives ingredients selected from the group consisting of testosterone, nitroglycerine, and nicotine. Although the examiner suggest restructuring the claim for clarity purposes since "two components" is confusing, this is not required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 5, 10-11, 15, 17-18, and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Sanvordeker et al (5,047,244).

Sanvordeker et al discloses a mucoadhesive carrier for the delivery of therapeutic agents. Figure 2 and 3 disclose a system that comprises component A) a impermeable barrier film, component B) a polymeric matrix with perforations to embed a retrieving element, and component D) a protective envelope. See Figures and column 9, lines 10-32. The polymeric matrix contains water-insoluble active agents (testosterone, estradiol, nifedipine) and is combined with polyethylene glycol (water-soluble polymer). See column 3, lines 45-60. The mucoadhesive carrier is combined with the active agent as a dispersion or solution. See column 4, lines 22-30. The mucoadhesive carrier is also combined with other hydrophilic polymers (hydroxylpropylcellulose methyl cellulose, hydroxylmethylcellulose). See examples. The PEG is melted at a temperature of 70 degrees and the powdered therapeutic agent is stirred in. The liquid composition is then poured onto a flattened surface and freeze-dried. The composition is then ground into a powder and mixed with other matrix forming hydrophilic (Klucel) and hydrophobic excipients. The resulting dried preparation of the polymer matrix is then compressed to the barrier film. See column 8, lines 5-55 and examples.

Note although the prior art does not explicitly state an immobilized active droplet, it is the examiner's position that the active agent of the prior art is inherently immobilized in the water-soluble polymer (PEG) after it is freeze-dried and then the PEG/active combination is again dried in other hydrophilic polymers. Lastly, the limitation "to be delivered in a surge upon breakdown of the polymer layer" is an intended use and if the prior art is capable of said

intended use, it is said to read on the limitation. In instant case, the prior art structure is the same as the instant inventions and thus is capable of performing the intended use.

Claims 1, 4, 8, 10-14, 18, 20, 22, 24, 26-27, and 29 are rejected under 35 U.S.C. 102(b) as being anticipated by Govil et al (5,262,165).

Govil teaches a transdermal nitroglycerin patch with penetration enhancers. The transdermal patch contains A) one or more backing layers, B) a polymeric matrix, C) an adhesive matrix, and, an optional rate controlling lining membrane, and D) a release liner. See column 5, lines 25-33. The backing layer is made of a water resistant material selected from polyester, polyethylene, vinyl, and metal foil. See column 5, lines 34-41. The adhesive utilized in the patch system is a pressure sensitive polymeric adhesive, which is 5-10 mils thick (127-254 um). See column 5, lines 42-50. The polymeric matrix is made of water-soluble material selected from gelatin, polyvinyl alcohols, PVP, Klucel (cellulose ether). See column 6, lines 4-10. The protective release liner is utilized to prevent dirt from sticking to the patch and is made from polyethylene or polyethylene coated paper and silicon-coated material. See column 6, lines 15-20. Example 5 discloses the polymeric matrix that contains glycerin, polyvinyl alcohol, PVP, nitroglycerin, oleic acid, and water. The glycerin and water is mixed and heated to 90 degrees C; after reaching 70 degrees C, the PVP and polyvinyl alcohol is added and stirred. Then the oleic acid and nitroglycerin are added and mixed. The mixture is then poured for a thickness of 3-4mm and the matrix is dried for 10-60 minutes and adhered to the backing material.

Note although the prior art does not explicitly state an immobilized active droplet, it is the examiner's position that the nitroglycerin of the prior art is inherently immobilized in the polymer layer after it is dried. Further, the process fro making the instant transdermal and the

prior's art method are the same, thus this further substantiates the examiner's position that the active ingredient is indeed immobilized in the water-soluble polymers. It should also be noted that nitroglycerin and oleic acid are both lipophilic and thus reads on the limitation "is not miscible with water." Lastly, the limitation "to be delivered in a surge upon breakdown of the polymer layer" is an intended use and if the prior art is capable of said intended use, it is said to read on the limitation. In instant case, the prior art structure is the same as the instant inventions and thus is capable of performing the intended use.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 17, 19, and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Govil et al (5,262,165).

As set forth above, Govil teaches a transdermal nitroglycerin patch with penetration enhancers. The transdermal patch contains A) one or more backing layers, B) a polymeric

matrix, C) an adhesive matrix, and, an optional rate controlling lining membrane, and D) a release liner. See column 5, lines 25-33. The backing layer is made of a water resistant material selected from polyester, polyethylene, vinyl, and metal foil. See column 5, lines 34-41. The adhesive utilized in the patch system is a pressure sensitive polymeric adhesive, which is about 5-10 mils thick (127-254 um). See column 5, lines 42-50. The polymeric matrix is made of water-soluble material selected from gelatin, polyvinyl alcohols, PVP. See column 6, lines 4-10. The protective release liner is utilized to prevent dirt from sticking to the patch and is made from polyethylene or polyethylene coated paper and silicon-coated material. See column 6, lines 15-20. Example 5 discloses the polymeric matrix that contains glycerin, polyvinyl alcohol, PVP, nitroglycerin, oleic acid, and water. The glycerin and water is mixed and heated to 90 degrees C; after reaching 70 degrees C, the PVP and polyvinyl alcohol is added and stirred. Then the oleic acid and nitroglycerin are added and mixed. The mixture is then poured for a thickness of 3-4mm and the matrix is dried for 10-60 minutes and adhered to the backing material.

Govil does teach the instant adhesive layer thickness of claim 19, the instant cellulose derivatives, or the method of treating angina.

It is deemed obvious to one of ordinary skill in the art at the time the invention was made to look to the guidance provided by Govil and manipulate the thickness of the adhesive layer. One would have been motivated to do so since Govil teaches that it is preferable to have a thickness of about 5 to 10 mils (127-254 um); however it is obvious to a skilled artisan to find the best optimum range of thickness through routine experimentation. Further, absent the criticality of the instant cellulose derivative, it is within the skill of an artisan to utilize any water-soluble cellulose polymer in the polymeric matrix of the Govil.

Lastly it would have been obvious to utilize Govil's transdermal to treat angina since Govil teaches nitroglycerin's effect in vasodilation of the blood vessels. Thus, although angina is not explicitly taught, it is obvious to a skilled artisan that Govil's nitroglycerin patch would treat angina since treatment of angina involves the dilation of the coronary vessels to provide relief.

Claims 5 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Govil et al (5,262,165) in view of Cardinal (4,601,893).

As set forth above, Govil teaches a transdermal nitroglycerin patch with penetration enhancers. The transdermal patch contains A) one or more backing layers, B) a polymeric matrix, C) an adhesive matrix, and, an optional rate controlling lining membrane, and D) a release liner. See column 5, lines 25-33. The backing layer is made of a water resistant material selected from polyester, polyethylene, vinyl, and metal foil. See column 5, lines 34-41.

Govil does not teach perforations in the polymeric matrix.

Cardinal teaches a laminate device for prolonged release. Cardinal teaches the use of macroperforations to provide a given release rate of the drug. See column 4.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Govil and Cardinal and utilize perforations in the polymer layer. One would have been motivated to do so since Cardinal teaches the use of perforations and the number of perforations provide for a desired release rate of the drug form the polymeric matrix. Thus, one would have been motivated to utilize perforations to manipulate the release rate of the drug.

Claims 17, 21, 23, and 28 rejected under 35 U.S.C. 103(a) as being unpatentable over Govil et al (5,262,165) in view of Wick et al (5679373).

As set forth above, Govil teaches a transdermal nitroglycerin patch with penetration enhancers. The transdermal patch contains A) one or more backing layers, B) a polymeric matrix, C) an adhesive matrix, and, an optional rate controlling lining membrane, and D) a release liner. See column 5, lines 25-33. The backing layer is made of a water resistant material selected from polyester, polyethylene, vinyl, and metal foil. See column 5, lines 34-41. The adhesive utilized in the patch system is a pressure sensitive polymeric adhesive, which 0is 5-10 mils thick (127-254 um). See column 5, lines 42-50. The polymeric matrix is made of water-soluble material selected from gelatin, polyvinyl alcohols, PVP. See column 6, lines 4-10. The protective release liner is utilized to prevent dirt from sticking to the patch and is made from polyethylene or polyethylene coated paper and silicon-coated material. See column 6, lines 15-20. Example 5 discloses the polymeric matrix that contains glycerin, polyvinyl alcohol, PVP, nitroglycerin, oleic acid, and water. The glycerin and water is mixed and heated to 90 degrees C; after reaching 70 degrees C, the PVP and polyvinyl alcohol is added and stirred. Then the oleic acid and nitroglycerin are added and mixed. The mixture is then poured for a thickness of 3-4mm and the matrix is dried for 10-60 minutes and adhered to the backing material.

The references do not teach the use of the instant cellulose water-soluble polymers, the instant silicone coated paper release liner, and nicotine as the active ingredient.

Wick et al teach a transdermal patch that has a backing layer, a release layer, an adhesive layer, and a drug layer (Note Figure). Wick teaches the active agent permeable adhesive layer to be dermatologically acceptable such as cellulose derivatives such as methylcellulose, ethylcellulose, PVP, polyvinyl alcohol, gelatin, among others which permits drug migration (col.16, line 59 to col. 17, line19). Further, Wick teaches conventional backing materials include

polyethylene terephalate, metal film, polyethylene, etc. See column 14, lines 55-66. Further, Wick teaches the use of nicotine as a transdermal active.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Govil and Wick and utilize the instant materials in the transdermal system of Govil's. One would have been motivated to do so since Wick et al teach that the instant water-soluble polymers and backing material are conventional materials utilized in the art. Further, Wick teaches methylcellulose, Govil's PVP, gelatin, polyvinyl alcohols, are all dermatologically acceptable to the skin of the host. Wick teaches polyethylene terephalate and Govil's metal foil and polyethylene are all utilized for backing material. Therefore, one would have been motivated to substitute Govil's material with instant materials with the expectation of success.

Lastly, it is obvious to replace one transdermal active agent such as nicotine for another active agent that is also capable of transdermal administration.

Claims 15, 30, and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Govil et al (5,262,165) in view of Place et al (5242391).

As set forth above, Govil teaches a transdermal nitroglycerin patch with penetration enhancers. The transdermal patch contains A) one or more backing layers, B) a polymeric matrix, C) an adhesive matrix, and, an optional rate controlling lining membrane, and D) a release liner.

The references do not teach the specific combination of testosterone and nitroglycerin.

Place et al teach the treatment of erectile dysfunction. On column 3, a line 12-20, Wick discloses the use of testosterone for the treatment of impotence in the prior art. Place teaches the topical application of nitroglycerin to treat impotence (col. 4, lines 30-51).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teaching of Govil and Place et al use a mixture of nitroglycerin and testosterone in a transdermal system. One would have been motivated to utilize both nitroglycerin and testosterone both for treating impotence with the expectation of an additive effect since both are independently taught to treat impotence.

Conclusion

None of the claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is 571-272-0614. The examiner can normally be reached on M-F (8:00-5:30), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sharmila S. Gollamudi
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